SIMULATION OF PROPAGATION IN A REALISTIC-GEOMETRY COMPUTER HEART MODEL WITH PARALLEL PROCESSING

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Abstract – **The simulation of the propagation of electrical activity in a realistic-geometry computer model of the ventricles of the human heart using the governing reaction-diffusion equation is described. Each model point is represented by the phase 1 Luo-Rudy membrane model, appropriately modified to represent human action potentials. A separate longer-duration action potential waveform was used for the M cells found in the ventricular mid-wall. Cardiac fiber rotation across the ventricular wall was implemented via an analytic equation, resulting in a spatially-varying anisotropic conductivity tensor and consequently anisotropic propagation. Since the model comprises approximately 12 million points, parallel processing was used to cut down on simulation time. The model generated acceptably-normal electrocardiograms, vectorcardiograms and body surface potential maps on the surface of a numerical human torso model. Interestingly, it was found that the intrinsic difference in action potential duration between M cells and other myocardial cells was greatly diminished due to electrotonic coupling.**
Keywords – **Heart model, reaction-diffusion equation, parallel processing, anisotropy, M cell, electrocardiogram**

I. INTRODUCTION

Computer models have long been used for the simulation of electrical activity in the heart. Many of these propagation models were of the cellular automaton type, simulating the electrical activity of the model cells with a ruled-based algorithm, e.g. Lorange and Gulrajani [1]. An exception was the model of Leon and Horáček [2] that used subthreshold electrotonic conduction to bring the cells to threshold, with subsequent action potential generation and refractory period determination being ruled-based. Only Huiskamp [3] recently described a ventricular heart model in which both subthreshold and suprathreshold activity were determined by modified Beuler-Reuter membrane equations [4]. We present here a similar heart model in which each model cell is represented by a modified version of the more accurate phase 1 Luo-Rudy [5] membrane equation. Since the spatial resolution is greater than that of Huiskamp's model (0.25 mm as opposed to 0.6 mm), simulations with the much larger number of points (approximately 12 million as opposed to 800,000 in Huiskamp's model) necessitated parallel processing on a multiprocessor computer.

II. METHODOLOGY

The resolution of the problem was done in two steps: the propagation of the electrical activity in the heart was simulated first, then the determined transmembrane potentials were used to calculate the torso surface potentials.

A. Simulation of Propagation

The propagation of electrical activity was simulated in the ventricles of the human heart model developed by Lorange and Gulrajani [1]. The ventricular myocardium can be represented by two continuous domains, intracellular and interstitial, characterized by the equations,

$$\nabla \cdot \left(\overline{G}_i \nabla \phi_i\right) = \beta I_m - \beta I_{stim} \tag{1}$$

$$\nabla \cdot \left(\overline{G}_e \nabla \phi_e\right) = -\beta I_m \tag{2}$$

respectively. Here ϕ_i and ϕ_e are the intracellular and interstitial potentials, respectively, $\overline{G}_i$ and $\overline{G}_e$ the intracellular and interstitial conductivity tensors, β the surface to volume ratio of the cardiac cells, I_{stim} the intracellular stimulation current, and I_m the transmembrane current coupling the two domains. I_m passes from the intracellular to the interstitial space and is the sum of the ionic and capacitive currents:

$$I_m = C_m \frac{\partial V_m}{\partial t} + I_{ion} \tag{3}$$

where C_m is the specific membrane capacitance ($C_m = 1$ $\mu F/cm^2$) and V_m is the transmembrane potential ($V_m = \phi_i - \phi_e$). The combination of equations (1), (2) and (3) and the approximation of equal anisotropy in the intracellular and interstitial spaces ($\overline{G}_i = \xi \overline{G}_e$) results in the reaction-diffusion equation:

$$\frac{\partial V_m}{\partial t} = \frac{1}{\beta C_m}\left[\frac{\xi}{1+\xi}\nabla \cdot \left(\overline{G}_e \nabla V_m\right) - \beta I_{ion} + \frac{\beta}{1+\xi} I_{stim}\right] \tag{4}$$

As mentioned, the dynamics of the ionic currents were based on the Luo-Rudy [5] membrane model. The action potential duration was, however, modified to match that of human ventricular cells. Two different action potential durations were used, a longer one for the so-called M cells [6] situated in the mid-ventricular walls and a shorter one for endocardial and epicardial

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Abstract

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cells. These changes were realized by decreasing the time constants τ_d and τ_f, responsible for the slow inward current I_{si} by a factor of 1.6 for the M cells, and by a factor of 2.0 for the endocardial and epicardial cells. Furthermore, the potassium conductance G_{K1}, responsible for the time-independent potassium current I_{K1}, was diminished for the M cells. These changes produce a transmural gradient of transmembrane potential during repolarization that contributes to the upright T waves noted in the normal electrocardiogram (ECG).

The propagation of electrical activity starts at the transition points between the Purkinje fibers and the myocardium; these points are stimulated at predetermined times. The propagation is more rapid along the cardiac fibers since myocardial anisotropy is included in the model. The fiber orientations are defined analytically with a modification of the Beyar and Sideman [7] equation. The longitudinal and transverse interstitial conductivities along and across fiber directions are 2.22 mS/cm and 1.33 mS/cm [8]. Intracellular conductivities are half these values as ξ was taken as 0.5.

Finite differences were used to solve equation (4). The temporal component was solved with the forward Euler method. The method of Victorri *et al.* [9] and the use of table look ups permitted rapid determination of the Luo-Rudy ionic currents. The formulation of Salaheen and Ng [10] was used for the calculation of the anisotropic diffusion current given by the first term on the right in equation (4). A time step of 25 μs was used during the action potential upstroke; this was increased to 50 μs during the plateau. The crossover from one time step to the other occurred when all model points terminated their upstrokes. The value of β was adjusted to control the total excitation time. Table I presents the parameters used to solve equation (4).

TABLE I
SIMULATION PARAMETERS

Parameter	Symbol	Value
Stimulus current	I_{stim}	200 μA cm^{-2}
Spatial step	Δx	250 μm
Membrane capacitance	C_m	1 μF cm^{-2}
Surface to volume ratio	β	333 cm^{-1}
Equal-anisotropy factor	ξ	0.5
Longitudinal interstitial conductivity	g_{el}	2.22 mS cm^{-1}
Transverse interstitial conductivity	g_{et}	1.33 mS cm^{-1}
Small time step	Δt_1	25 μs
Large time step	Δt_2	50 μs

The propagation of electrical activity was simulated on a Silicon Graphics Origin 2000 parallel computer consisting of 64 R12000 processors operating at 400 MHz. Running the simulation on the 8 processors accessible to us took 20 hours. The use of finite differences allowed an easy separation of the problem into portions that could be handled simultaneously on different processors. Total simulation time depends mainly on the time spent to calculate the nodal ionic currents, and using the full bank of 64 processors would likely cut simulation time by very nearly a factor of 8.

B. Torso Surface Potentials

The spatial gradient of the transmembrane potential distribution determined from equation (4) was used to calculate elemental current dipoles at each model point. This assumes the approximation of an isotropic myocardium, and results in dipoles that are everywhere normal to the excitation wavefront. The elemental dipoles were combined into 58 regional dipoles that, in conjunction with a human torso model, were then used to calculate the torso surface potentials using standard integral equation approaches [11].

III. RESULTS

Following initial adjustment, the heart model generated an acceptably-normal ECG (Fig. 1). Also verified to be normal were the vectorcardiogram and the body surface potential map. Note the largely upright T waves in the ECG of Fig. 1, and as mentioned this was realized largely by the presence of the M cells in the ventricular walls, with their longer action potential durations.

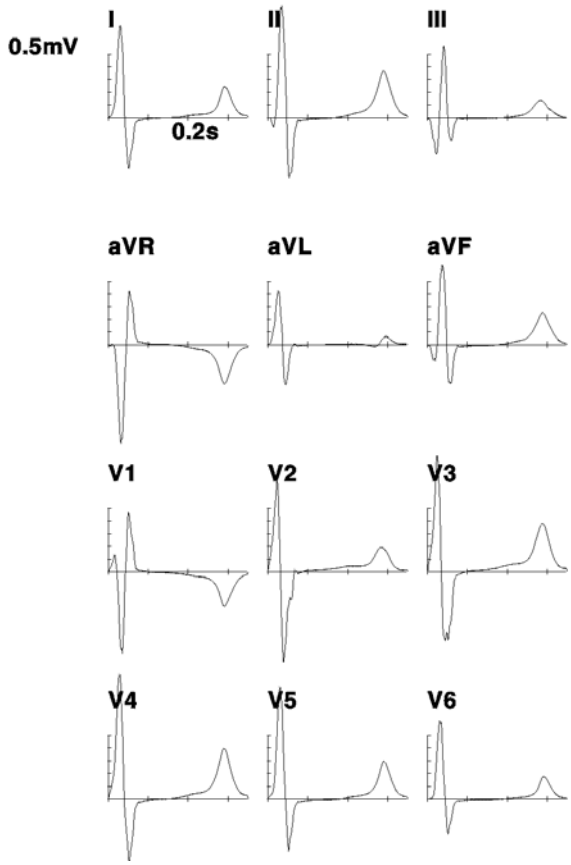

Fig. 1: The simulated normal ECG. Depolarization (QRS) and repolarization (T wave) are both shown.

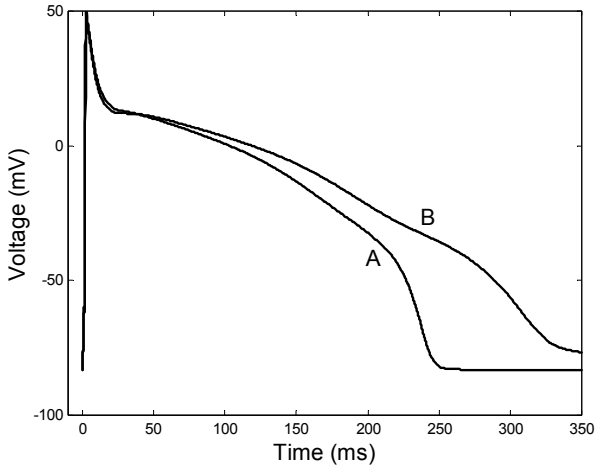

Fig. 2: Action potential waveforms for A) endocardial or epicardial cells and B) M cells.

TABLE II
ACTION POTENTIAL DURATION ACROSS THE LEFT VENTRICULAR WALL

Endocardial cell	M cell	Epicardial cell
274 ms	310 ms	255 ms

Fig. 2 shows the intrinsic action potential durations of the M cells as well as those of the endocardial or epicardial cells. There is an intrinsic difference in action potential duration of approximately 80 ms. During simulation, however, this intrinsic difference was greatly diminished by the electrotonic coupling introduced between adjacent cells by equation (4). Table II gives the action potential durations measured at one site across the left ventricular wall during normal excitation. It is seen that the intrinsic difference in action potential durations drops from 80 ms to approximately 35-55 ms.

IV. DISCUSSION

We have demonstrated the feasibility of simulating normal activation of the ventricles using the reaction-diffusion equation (4), together with an accurate membrane model for the ventricular cells. The simulated ECG of Fig. 1 is close to a normal ECG. Even more interesting is the demonstration of the reduction in intrinsic action potential durations across the ventricular wall due to electrotonic coupling. Anyukhovsky et al. [12] noted that the difference in action potential durations between M cells and endocardial/epicardial cells was greater in vitro than in situ, and suggested that this was due to electrotonic coupling. Verification of this electrotonic coupling hypothesis is difficult experimentally, but as evidenced by the above results, is easy to accomplish via computer simulation.

In order to cut down on computation time, we used the simple criterion of switching from the 25 μs to the 50 μs time step once the upstroke terminated at all model points. This criterion is easily implemented for the simulation of a single normal beat. When simulating arrhythmias, however, multiple disparate wavefronts from consecutive beats may coexist at any given time instant, and a more sophisticated space-time wavefront tracking algorithm is needed to determine where and when the time step needs to be switched. One such adaptive tracking algorithm was proposed recently by Cherry et al. [13], and the incorporation of such an algorithm into the model is essential in order to render it truly versatile.

V. CONCLUSIONS

The use of the more physiologically-correct reaction-diffusion equation (4) and the Luo-Rudy membrane model [5], together with two types of action potential waveforms, allows for more realistic ECG simulations. This kind of large-scale simulation is only feasible with parallel processing rather than with conventional serial computing. We have demonstrated the computation of the normal ECG. The next step is to implement a more sophisticated wavefront tracking algorithm into the model in order to be able to simulate cardiac arrhythmias.

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